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Using Satellite-Based Spatiotemporal Resolved Air Temperature Exposure to Study the Association between Ambient Air Temperature and Birth Outcomes in Massachusetts

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Running title: Air temperature birth weight and gestational age

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Abstract

Background: Studies looking at air temperature (*Ta*) and birth outcomes are rare.

Methods: We evaluated birth outcomes and average daily *Ta* during various prenatal exposure periods in Massachusetts (USA) using both traditional *Ta* stations and modeled address *Ta*. We used linear and logistic mixed models, and accelerated failure time models, to estimate associations between *Ta* and the following outcomes among live births > 22 weeks: term birth weight (≥ 37 weeks), low birth weight (LBW) (< 2,500g at term), gestational age and preterm delivery (PT) (< 37 weeks). Models were adjusted for individual level socioeconomic status, traffic density, $PM_{2.5}$, random intercept for census tract and mothers health.

Results: Predicted *Ta* during multiple time windows before birth was negatively associated with birth weight: average birth weight was 16.7g lower (95% CI: –29.7, –3.7) in association with an IQR increase (8.4°C) in *Ta* during the last trimester. *Ta* over the entire pregnancy was positively associated with PT (OR = 1.02; 95% CI: 1.00, 1.05) and LBW (OR = 1.04; 95% CI: 0.96, 1.13).

Conclusions: *Ta* during pregnancy was associated with lower birth weight and shorter gestational age in our study population.

Background

The increase in temperatures over the last century and continued increases in emissions of greenhouse gases has focused attention on the effects of increasing heat (Crowley 2000). Relatively few studies have examined associations between average daily ambient air temperature during pregnancy (*Ta*) and pregnancy outcomes. Most published work has focused on the relationship between preterm delivery and *Ta* with variable results. One study reported an increased risk of very low-birth weight (LBW) delivery (birth weight < 1500 grams) with colder ambient temperature (Hartig and Catalano 2013). Another study found no association between preterm birth (birth at < 37 weeks completed gestation) and a variety of factors including temperature, humidity and barometric pressure (Lee et al. 2008). In contrast, two studies have reported that preterm delivery was associated with increased temperature and humidity (Basu et al. 2010; Lajinian et al. 1997). A study conducted in Australia reported that weekly temperature was positively associated with preterm birth < 37 weeks and stillbirth < 36 weeks gestation (Strand et al. 2012). Schifano and colleagues reported that maximum apparent temperature in the two days preceding delivery was associated with preterm delivery in Rome during the warm season using models adjusted for air pollution, socioeconomic status and mothers health (Schifano et al. 2013).

It is important to determine if ambient temperature indeed affect the length of gestation and birth weight at delivery, as low-birth weight delivery has significant short and long-term health implications. Preterm delivery (delivery at < 37 weeks gestation), early term delivery (delivery at 37-38 weeks gestation) and in utero growth restriction (IUGR, or delivery at birth weight < 10^{th} percentile for gestational age) also contribute to perinatal morbidity and mortality (Harding and Maritz 2012; McCormick 1985; Moster et al. 2008; Sengupta et al. 2013). Evidence suggests that

IUGR birth in particular may have long-term implications for childhood and adult health (Bilbo and Schwarz 2009; Demicheva and Crispi 2013; Gluckman and Hanson 2004; Harding and Maritz 2012; Sarr et al. 2012; Vos et al. 2006). The pathogenesis of preterm, early term and IUGR delivery is multifactorial. Inflammation, infection and immune dysregulation may cause preterm labor and early delivery; abnormalities of placental formation and function may result in preterm, early term and IUGR delivery due to placental bleeding, fetal distress and pre-eclampsia; and genetic variation and multiple gestation contributes to each of these etiologies (Gonçalves et al. 2002; Han et al. 2011; Leber et al. 2010; Muglia and Katz 2010; Saito et al. 2010; Wong and Grobman 2011). Social stressors have also been studied as causes of preterm, early term and IUGR delivery, due to variation in the rate of low-birth weight delivery among different racial, ethnic and socioeconomic groups (Kuzawa and Thayer 2011; Wadhwa et al. 2011). Environmental stressors such as changes in ambient air temperature may also contribute to these birth outcomes. A recent study by Dadvand and colleagues (Dadvand et al. 2014) examined the association of term low birth weight with residential proximity to major roads and surface temperature. They showed that living within 200 m of major roads was associated with a increase in term LBW risk (OR = 1.46; 95% CI: 1.05, 2.04). They also found that surface temperature was associated with an increase in term LBW risk (OR = 1.18; 95% CI: 0.95, 1.45). The conflicting results published to date on relationship of ambient air temperature to preterm and/or low birth weight delivery may be due to variations in temperature measurement and modeling. Air temperature stations have limited spatial coverage, particularly in less urban areas, and airport monitors may not reflect the urban heat island adequately. Since temperature can vary greatly both spatially and temporally, the use of air temperature stations can introduce considerable measurement error (and downward bias in the case of heat islands) reducing their utility for epidemiological studies on the health effects of extreme temperature and climate change. Previous studies examining the association of preterm and low-birth weight delivery and *Ta* have typically used available monitors in the study area. This introduces exposure error and likely biases the effect estimates downward (Armstrong 1998; Zeger et al. 2000). Furthermore, lack of spatially resolved daily *Ta* concentration data restricts these studies to populations surrounding monitoring sites, which may not be representative of the population as a whole.

The lack of high resolution continuous spatio-temporal *Ta* data resulted in our group developing a method to predict 24h mean *Ta* at a very fine spatial resolution (Kloog et al. 2012a, 2014). Specifically, we developed new methodologies to predict daily *Ta*, based on land use regression plus a daily calibration of *Ta* ground measurements and MODIS (Moderate Resolution Imaging Spectroradiometer, http://modis.gsfc.nasa.gov/data/) surface temperature (*Ts*) over a large area with varying geographical characteristics (covering the entire Northeast and Mid-Atlantic areas of the USA) at a 1x1 km spatial resolution. We incorporated land use, and meteorological variables to predict daily 24h mean *Ta* for grid cells even when satellite *Ts* measures are not available. A similar model has previously been developed for $PM_{2.5}$ on the same resolution (Kloog et al. 2012c).

We used our Ta prediction data to study associations between Ta and live birth outcomes among singleton births in Massachusetts during 2000–2008, including term birth weight, low birth weight (< 2500 g) among term births, preterm birth (< 37 weeks), and gestational age.

Methods

Study domain and population

In the analysis we included the entire state of Massachusetts (Figure 1). The study population included all live singleton births >22 weeks of gestation in Massachusetts from January 1, 2000 through December 31, 2008 (Figure 1). Birth data and the latitude and longitude of each eligible address at birth were provided by the Massachusetts Birth Registry (MBR, http://www.mass.gov/eohhs/gov/departments/dph/programs/admin/dmoa/vitals/). The term birth weight and low birth weight (< 2,500 g) analyses included 453,658 births ≥ 37 weeks gestational age, and the gestational age and preterm birth (<37 weeks) analyses included 473,977 births. The study and the use of birth data was approved by the Massachusetts Department of Public Health and the human subjects committee of the Harvard School of Public Health. Informed consent was not required because we used anonymous administrative data.

Exposure data

For exposure data we used three different indicators: predicted 1x1 km *Ta* from our model, ground *Ta* from the nearest National Climatic Data Center (NCDC, http://www7.ncdc.noaa.gov/CDO/) monitoring stations, and residence-specific cumulative traffic density. We describe each metric in more detail below.

Predicted Air temperature - *Ta* exposure data were generated by the previously mentioned *Ta* prediction model (Kloog et al. 2014) In these prediction models we used mixed models to first calibrate *Ts* and *Ta* measurements, regressing *Ta* measurements against day-specific random intercepts, fixed and random *Ts* slopes and several spatial and temporal predictors (NDVI-Normalized difference vegetation index, percent urban and elevation). Then to make use of the ability of neighboring cells to fill in the cells with missing *Ts* values, we regressed the *Ta* predicted from the first mixed effects model against the mean of the *Ta* measurements on that day from monitors within 60 km, separately for each grid cell. We used ten-fold out of sample cross validation (CV) to validate our predictions at monitor locations at each step. We randomly divide our data into 90 and 10 percent splits ten times. We predict for the 10% data sets using the model fitted from the remaining 90% of the data. We then report these computed R2 values. To test our results for bias we regress the measured Ta values against the predicted values in each site on each day. We estimated the model prediction precision by taking the square root of the mean squared prediction errors (RMSPE). Mean out-of-sample R^2 values for days with and without Ts data were 0.947 and 0.940, respectively, indicating excellent model performance. Mean out-of-sample temporal and spatial R2 values also were high (0.956 and 0.832, respectively) (Kloog et al. 2014).

To estimate Ta exposure we linked each mother's residence at the time of delivery to its corresponding grid cell (Figure 2). Daily Ta exposures were calculated for the day of birth; the day before birth; moving average values for 3 days, 7 days, 14 days, 30 days, the last trimester; and the entire pregnancy.

$PM_{2.5}$- $PM_{2.5}$ was estimated on a 1x1 km grid from the same MODIS satellite, using daily measures of Aerosol Optical Depth using a similar methodology (daily calibration, land use and meteorology) as the temperature model. Further details have been published previously (Chudnovsky et al. 2014; Kloog et al. 2012c). Because warm days are often more polluted, $PM_{2.5}$ was included as a covariate with the same time periods used to classify Ta.

Monitor Air temperature - Daily data for monitor *Ta* across Massachusetts were obtained from the NCDC. NCDC is a government agency and has been collecting meteorological data for close to a century now. *Ta* is measured at a reference height of 2m above the ground in most weather stations (NCDC 2010). .

Cumulative traffic density- Traffic emissions have been associated with birth outcomes in many previous studies (Gryparis et al. 2009; Zeka et al. 2006). Therefore, Massachusetts road data (average daily traffic-ADT) were obtained from the Massachusetts Department of Transportation (MassDOT,http://www.massdot.state.ma.us/) 2002 Road inventory. These data are based on automatic vehicle counts on major highways, periodic counts on other major roads and estimated counts for all other roads. (Kloog et al. 2012b). Each 200x200 grid was assigned a value for normalized cumulative ADT (CADT) based on average daily traffic on all road segments within 100 m of the center of each grid, where CADT = Σ (ADT*road segment length). Each birth address was assigned the average CADT value for the four grids with center points closest to the address, using bilinear interpolation .

Based on previous literature on the potential risk factors associated with low birth weight (Kloog et al. 2012b; Zeka et al. 2006, 2008) we included the following individual and contextual covariates:

Percent of open space- The percent of open space data was obtained from the office of geographic information Commonwealth of Massachusetts, information technology division MassGIS (MassGIS-EOEA 2006). The subset of the open space designated for recreation and conservation was intersected with 2000 Census tract boundaries (also downloaded from

MassGIS) using ArcGIS© 10.1. The percent of each census tract that was open space was then calculated and assigned to birth addresses belonging to that tract.

Socioeconomic indicators- Socioeconomic data at the Individual level were obtained from the Massachusetts birth registry. Information included the mother's race/ethnicity (classified as Hispanic; non-Hispanic white, African American, and Asian; and other [all other ethnic groups]), mother's years of education, and the Kotelchuck index of adequacy of prenatal care utilization (APNCU). APNCU is based on the number and the time of start of mother's prenatal visits (Alexander and Kotelchuck 1996) and was recoded into: inadequate (<50% of expected visits used); intermediate (50–79%); appropriate (80–109%); and appropriate plus (≥110%). We categorized Education of the mother as: no high school (<9 years of educational attainment), some high school 9-12 years of educational attainment); some college (13–15 years); and college or postgraduate (≥ 16 years).

Median income- Data was obtained from the United States Census Bureau 1999 median household income (USCB 2000) for every census tract in the study area, and assigned these to births with an address located within that tract.

Individual-level covariates: maternal age, parity, gestational age (calculated by the maternal recall of last menstrual period), amount of cigarettes smoked per day during and before pregnancy, chronic conditions of mother or conditions of pregnancy (lung disease, pregnancy-induced hypertension, gestational diabetes and non-gestational diabetes all modeled separately as single variables), previous occurrence of a preterm birth, whether the mother ever had a previous infant weighing 4000 grams or more and sex of infant were all obtained through the Massachusetts Birth Registry through the index child's birth certificate.

Statistical methods

To identify factors affecting birth weight we used linear mixed regression models to estimate associations between both monitor and modeled Ta during different time windows and term birth weight, and logistic mixed regression to estimate associations with preterm birth (< 37 weeks) and low birth weight (< 2,500 g, LBW) (Kloog et al. 2012b; Zeka et al. 2008). Seasonality was controlled using sine and cosine terms with a period of 365.24 days. Both sine and cosine were included to allow the regression to estimate both the amplitude of the seasonal cycle and its phase. A random intercept for census tract was used to capture unmeasured similarities in persons residing in the same neighborhood.

Specifically we fit the following models:

$$BW_{ij} = (\alpha + u_j) + \beta_1 Ta_i + \beta_2 PM_i + \gamma \boldsymbol{X}_i + e_{ij} \quad (u_j) \sim N[0, \sigma_u^2] \quad \text{and} \qquad [1]$$

$$Logit(PT_{ij}/LBW_{ij} = 1|X) = (\alpha + u_j) + \beta_1 Ta_i + \beta_2 PM_i + \gamma \boldsymbol{X}_i + e_{ij} \quad (u_j) \sim N[0, \sigma_u^2] \qquad [2]$$

where BW_{ij}, PT_{ij}, and LBW_{ij} represent birth weight, preterm, and LBW, respectively, for the *i*th subject in census tract *j*, α and u_j are the fixed and random (tract-specific) intercepts, respectively, $\gamma \boldsymbol{X}_i$ denote the set of variables included in the model which include: predicted ambient air temperature, predicted ambient $PM_{2.5}$, cumulative traffic density, percent of open spaces, age of mother, median income, gestational age, chronic conditions of mother or conditions of pregnancy (lung disease, hypertension, gestational diabetes or non-gestational diabetes), parity, previous infant weighting 4000 grams and sex of infant, sine and cosine (controlling for seasonality), APNCU (as a categorical variable), mothers race (as a categorical variable), mothers education (as a categorical variable) and previous preterm occurrences. e_{ij} is the error term and finally, σ_u^2 is the variance of the tract random effects, and $e_{jj} \sim N[0, \sigma^2]$.

We estimated associations between Ta during different time windows and gestational age using an accelerated failure time model (AFT).

Such models are a form of survival analysis that model the survival time directly instead of the hazard. Gestational age is used as a continuous outcome in the AFT model. The log-linear form of the AFT model with respect to time (*T*) is given by

$$\log T_i = \mu + \alpha_1 X_{1i} + \alpha_2 X_{2i} + \ldots + \alpha_p X_{pi} + \sigma\varepsilon_i \qquad [3]$$

where μ is the intercept, σ is a scale parameter and ε_i is a random variable, assumed to have a particular distribution. We adopted a gamma distribution for ε_i, which can flexibly model a wide range of distributions for the failure times (births). A two-sided p-value < 0.05 was considered statistically significant.

We also ran analyses stratified on subject residence < 30 km or ≥ 30 km of a Ta monitor (as proxy indicators of urban and rural residences, respectively). Statistical analyses were performed in SAS (version 9.3; SAS Institute Inc., Cary, NC, USA) and R (R Foundation for Statistical Computing, Vienna, Austria). Cases with missing data were excluded from the analysis. An alpha level of 0.05 indicates statistical significance.

Results

Descriptive statistics are presented in Table 1. Of the 450,407 births included in all births in our analyses, 50% of the births were male, 72% were white, only 8% had maternal age below 20 for full term births and 21% of the mothers had more than 15 years of education. Mean birth weight was 3395 g ± 502 among term births and 3391 g ± 511 among all births. Table 2 contains a summary of the predicted *Ta* and traffic exposure across all grid cells in the analysis. Table 3 presents the IQR for each time window used in the analysis. Table 4 presents the results from the regression across all exposure periods tested for both the predicted exposures and monitor exposure analyses. Using our spatially and temporal resolved predicted *Ta* as exposure resulted in all exposure windows showing decreased birth weights with increased *Ta* with almost all exposure windows showing statistical significance. We observed a pattern of increasing impact of an interquartile range (IQR) change in temperature exposure with increasing averaging time up until the last trimester of gestation average. The effect for the full pregnancy was smaller than that of the last trimester moving average.

Term birth weights were negatively associated with predicted Ta in almost all exposure time windows (Table 4). In general, the average estimated difference in term birth weight with an 8.4ºC (IQR) increment in Ta increased as the averaging time increased up to the last trimester before birth, whereas associations were weaker for average exposure over the entire pregnancy. For example, average term birth weight was 8.9 g lower (95% CI: –16.2, –1.5) in association with an 9.0ºC IQR increase in Ta during the seven days before birth, 16.6 g lower (95% CI: –27.4, –5.9) and 16.7g lower (95% CI: –29.7, –3.7) for the 30 days and last trimester before birth respectively (IQR increase of 9.1ºC and 8.4ºC) and 5.0 g lower (95% CI: –7.8, –2.3) with an IQR increase of 2.7ºC in average Ta over the entire pregnancy.

The OR for low term birth weight with a 2.7ºC increase in model-based Ta over the entire pregnancy was 1.04 (95% CI: 0.96, 1.13), compared with 1.07 (95% CI: 0.87, 1.27) for monitor-based Ta (Table 5). The OR for preterm birth with a 2.7ºC increase in model-based Ta over the entire pregnancy was 1.04 (95% CI: 0.96, 1.13) compared with 1.02 (95% CI: 1.00, 1.05) for monitor-based Ta.

A 2.7ºC increase in Ta over the entire pregnancy was associated with a 0.26% decrease in gestational age (95% CI: –0.28, –0.25%), while A 8.4ºC increase in Ta over the last trimester before birth was associated with a 0.15% decrease in gestational age (95% CI: –0. 26, 0.05%) (Table 5). For monitor-based Ta the results were significant as well but showed an increase in gestational age: a 0.89% increase in gestational age (95% CI: 0.88, 0.90%) for full term birth and 0.37% increase in gestational age (95% CI: 0.37, 0.38%) for the last trimester.

The association between an IQR increase in predicted Ta during the entire pregnancy and birth weight was stronger among births to mothers with residences in "urban" areas (<30 km from a monitor, 8.1 g lower; 95% CI: –12.2, –4.0) compared with mothers residing in "rural" areas (>30 km from a monitor, 4.2 g lower; 95% CI: –8.4, 0.1), though the differences were not statistically significant (interaction p-value = 0.26).

Discussion

In the presented study we estimated the associations of *Ta* on birth outcomes in a study of singleton births in Massachusetts counties between 2000 and 2008. Using a model enhanced with satellite remote sensing we were able to assign exposure to all subjects with less spatial and temporal error (compared to using a closest monitor approach), regardless of the distance between a participant's residence and the closest *Ta* monitor.

We found a consistent negative association between Ta and birth weight for infants who were born full term after adjusting for other potential risk factors such as previous and current mother's health conditions, socioeconomic factors and physical environment risk factors such as traffic density in surrounding grid cells. The association with Ta over the entire pregnancy was stronger in more urban areas (<30 km from a monitor) than in more rural areas (≥ 30 km from a monitor), though the difference was not statistically significant. In contrast to the associations found with our modeled predicted *Ta*, associations between birth weight and *Ta* measured at the nearest ground monitor stations were close to the null, suggesting that predicted *Ta* classified exposure more accurately than monitor-based estimates. Interestingly, for the AFT analysis we found that an increase in *Ta* over both periods were associated with a decrease in gestational age yet in the monitored *Ta* analysis this associations were significantly associated with an increase of gestational age. These finding need to be further explored in future studies.

A key advantage of the presented study is the exposure assignment. Since our model allows us to predict temporally and spatially resolved *Ta* we can assign daily *Ta* exposure to the entire study population, avoiding potential selection bias that would yield a non-representative sample. It also captures the urban heat island effect, as shown in Figure 2. In addition we account for small area measures of potential confounders at a 1x1 km spatial resolution such as individual and census measures of SES, and medical history.

The literature on the potential impact of *Ta* on birth weight and its determinants are still far and few. Increased *Ta* may affect birth weight through direct or indirect means. The causes of preterm birth and low birth weight are largely unknown, but are likely to be a complex mix of genetic, behavioral, socioeconomic and environmental factors (Strand et al. 2011). Heat stress during spells of high *Ta* has been suspected as a cause of premature birth resulting in high prevalence of low birth weight (Basu et al. 2010). Pregnant women may be more susceptible to changes in temperature due to the extra physical and mental strain, and may be at a greater risk of heat stress because of multiple factors such as: increased fat deposition; the ratio of surface area to body mass which decreases, reducing the capacity to lose heat by sweating, weight gain which increases heat production and the fetus adding to the maternal heat stress by adding its own bodies composition and its own metabolic rate (Wells and Cole 2002). Three studies have reported positive associations between preterm birth and *Ta* (Flouris et al. 2009; Lajinian et al. 1997; Yackerson et al. 2008) but two other studies did not report an association (Lee et al. 2008; Porter et al. 1999).

Race, ethnicity, education and other SES factors are often clustered spatially and can act as potential confounders since they do not vary by time but do vary by space. We use a random-effects model with a random intercept for FIPS code while controlling for seasonality to reduce bias as well.

There are several limitations in the present study. First, the spatial resolution of the exposures was 1x1 km. As satellite remote sensing evolves and progresses, higher spatial resolution data should become available in the coming years, which will further reduce exposure error. Such increased resolution should enable us to more precisely estimate daily intra urban exposures and how these vary across spatial locations. Other limitations include the lack of some health and personal level data such as maternal weight, BMI, differences across different locations in physical activity, pollen exposure etc. that was not available. We also lacked data on indoor temperature exposure and information on air conditioning use in households. Finally, another limitation, which also should be mentioned, is the lack of information on road noise as in some recent pregnancy outcome studies (Dadvand et al. 2014; Gehring et al. 2014).

In summary, our findings suggest that higher Ta during pregnancy may be a risk factor for lower birth weight.

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Table 1. Characteristics of live births in Massachusetts during the 9 year period 2000–2008 for both the full term analysis and AFT models.

	Term births			All births ≥ 22 weeks		
Characteristic	**% All births (N)**	**Mean Birth Weight (g) ± SD**	**Missing**	**% All births (N)**	**Mean Birth Weight (g) ± SD**	**Missing**
Overall	(450,407)	3395 ± 502	3251	(462,400)	3391 ± 511	3381
Maternal race			0			0
White	72 (323,819)	3443 ± 496		72 (332,383)	3440 ± 503	
African-American	7 (33,775)	3257 ± 520		8 (34,803)	3246 ± 540	
Hispanic	13 (60,339)	3297 ± 496		13 (62,029)	3313 ± 522	
Asian	7 (31,491)	3234 ± 463		7 (32,174)	3229 ± 473	
Other	0.3 (983)	3347 ± 505		0.3 (1011)	3339 ± 527	
Maternal Education (years)			1699			1748
≤ 8	3 (12,718)	3293 ± 492		3 (13,121)	3288 ± 501	
>8-12	34 (154,723)	3319 ± 511		34 (159,307)	3313 ± 523	
13-15	42 (187,792)	3407 ± 503		42 (192,246)	3455 ± 491	
≥15	21 (94,994)	3457 ± 485		21 (97,726)	3403 ± 512	
Maternal age (years)			1			1
≤ 20	5 (22,900)	3219 ± 489		5 (23,618)	3211 ± 505	
20-29	33 (146,668)	3335 ± 518		33 (150,538)	3330 ± 504	
30-34	32 (142,033)	3427 ± 493		32 (145,720)	3424 ± 500	
35-39	24 (106,542)	3459 ± 518		24 (109,365)	3455 ± 512	
>39	7 (32,244)	3434 ± 518		7 (33,159)	3431 ± 530	
Maternal chronic conditions						
Gestational diabetes	3 (15,047)	3419 ± 633	1342	3 (15,388)	3407 ± 562	1420
Non-gestational diabetes	1 (3128)	3419 ± 633	1342	1 (3219)	3411 ± 649	1420
Previous infant ≤ 4 kg	1 (3503)	3936 ± 508	1342	1 (3594)	3937 ± 511	1420
Hypertension	3 (12,721)	3258 ± 567	1342	3 (13,038)	3253 ± 575	1420
Lung disease	3 (14,535)	3295 ± 531	1342	3 (14,906)	3287 ± 547	1420
Previous preterm birth	1 (4331)	3080 ± 576	1342	1 (4475)	3070 ± 593	1420
Gestational age (weeks)	(450,407)	39.0 ± 1.83	0	(462,400)	38.97 ± 1.95	0
APNCU			0			0
1 (Inadequate)	9 (40,427)	3309 ± 507		9 (41,692)	3304 ± 518	
2 (intermediate)	8 (35,519)	3438 ± 476		8 (36,559)	3438 ± 477	
3 (appropriate)	48 (215,188)	3465 ± 463		48 (222,638)	3465 ± 465	
4 (appropriate plus)	35 (159,273)	3312 ± 539		35 (163,511)	3304 ± 555	
Mean household Income	(453,658)	52,313 ± 21,566	0	(462,400)	52,296 ± 21,573	0
Sex			0			0
Male	50 (226,589)	3452 ± 511		50 (232,720)	3447 ± 521	
Female	50 (223,818)	3337 ± 486		50 (229,680)	3334 ± 494	
Parity (number of births)	(450,407)	2 ± 2.7	0	(462,400)	2 ± 2.7	0
Cigarettes per day during pregnancy (smokers)	(450,407)	0.6 ± 2.7	642	(462,400)	0.7 ± 2.7	656
Cigarettes per day before pregnancy (smokers)	(450,407)	1.8 ± 5.1	616	(462,400)	1.8 ± 5.1	631

	Term births			All births ≥ 22 weeks		
Characteristic	**% All births (N)**	**Mean Birth Weight (g) ± SD**	**Missing**	**% All births (N)**	**Mean Birth Weight (g) ± SD**	**Missing**
Cumulative traffic density (average daily traffic counts)	(450,407)	39.4 ± 23.5	0	(462,400)	39.2 ± 23.2	0
Elevation (meters)	(450,407)	59.9 ± 68.3	0	(462,400)	60 ± 68.4	0
Percent of open space	(450,407)	12.0 ± 11.1	0	(462,400)	12.0 ± 11.1	0
Season of Birth			0			0
Winter	22 (97,982)	3379 ± 504		24 (108,896)	3378 ± 514	
Spring	26 (117,669)	3402 ± 502		26 (118,182)	3399 ± 512	
Summer	27 (121,629)	3399 ± 501		26 (121,917)	3396 ± 510	
Fall	25 (113,127)	3393 ± 500		25 (113,405)	3390 ± 508	

Table 2. Descriptive statistics for daily air temperature, daily $PM_{2.5}$ exposure and traffic density across mother's residences (397,698) in Massachusetts between 2000–2008.

Covariate	Mean	Median	SD	Min	Max	IQR	25th percentile	75th percentile	Days of data available
Predicted Air temperature (C°)	11.3	11.4	5.6	-12.1	35.49	8.9	6.9	15.8	3285
Cumulative traffic density (daily traffic*length)	1309	702	2076	0	29,000	1352	258	1611	3285
Predicted $PM_{2.5}$ ($\mu g/m^3$)	10.9	9.27	5.9	0.2	56.9	6.8	6.7	13.5	3285

Table 3. IQR (interquartile range) values for each time window used in the study.

Exposure period	**IQR (ºC)**
Day of birth	8.9
One day prior to birth	8.9
Moving average of 3 days prior to birth	9.0
Last week (7 days prior to birth)	9.0
Last 2 weeks (14 days prior to birth)	9.0
Last month (30 days prior to birth)	9.1
Last Trimester	8.4
Entire pregnancy	2.7

Table 4. The adjusted association between a one interquartile range increase in air temperature (C°) and $PM_{2.5}$ and birth weight for full term births at various exposure periods (n=453,658).

Exposure period	**Predicted Air temperature (C°) β (95% CI)**	**Closest monitor temperature (C°) β (95% CI)**
Day of birth	-3.6 (-8.1, 0.9)	0.6 (-4.8, 6.0)
One day prior to birth	-4.4 (-9.6, 0.7)	1.8 (-3.8, 7.5)
Moving average of 3 days prior to birth	-4.1 (-9.8, 1.5)	3.0 (-2.8, 8.8)
Last week (7 days prior to birth)	-8.9 (-16.2, -1.5)	1.5 (-4.6, 7.7)
Last 2 weeks (14 days prior to birth)	-15.5 (-24.2, -6.8)	0.5 (-6.4, 7.3)
Last month (30 days prior to birth)	-16.6 (-27.4, -5.9)	2.0 (-6.3, 10.2)
Last Trimester	-16.7 (-29.7, -3.7)	-8.0 (-20.3, 4.3)
Entire pregnancy	-5.0 (-7.8, -2.3)	2.6 (-17.1, 22.4)

All models adjusted for: Predicted Air temperature, Predicted $PM_{2.5}$, cumulative traffic density, percent of open spaces, age of mother, gestational age, chronic conditions of mother or conditions of pregnancy (lung disease, hypertension, gestational diabetes or non-gestational diabetes), parity, previous infant weighting 4000 grams and sex of infant, sine and cosine (controlling for seasonality), APNCU (as a categorical variable), mothers race (as a categorical variable), mothers education (as a categorical variable) and previous preterm occurrences

Table 5. Accelerated failure time model (AFT) results on the relationship between gestational age and *Ta* (*n*=473,977) and logistic model results on preterm (*n*=473,977) and low birth weight outcomes (*n*=453,658).

Outcome and exposure time period	**Predicted Air temperature (C°)**	**Closest monitor temperature (C°)**
AFT model (Gestational period) Beta (95% CI)		
Last Trimester	-0.0015 (-0.0026, 0.0005)	0.0037 (0.0037, 0.0038)
Entire pregnancy	-0.0026 (-0.0028, -0.0025)	0.0089 (0.0088, 0.0090)
Preterm births (< 37 weeks) [OR (95% CI)]		
Entire pregnancy	1.02 (1.00, 1.05)	1.07 (0.87, 1.27)
Low birth weight (< 2,500 g) [OR (95% CI)]		
Entire pregnancy	1.04 (0.96, 1.13)	1.02 (0.45, 2.30)

All models adjusted for: Predicted Air temperature, Predicted $PM_{2.5}$, cumulative traffic density, percent of open spaces, age of mother, chronic conditions of mother or conditions of pregnancy (lung disease, hypertension, gestational diabetes or non-gestational diabetes), parity, previous infant weighting 4000 grams and sex of infant, sine and cosine (controlling for seasonality), APNCU (as a categorical variable), mothers race (as a categorical variable), mothers education (as a categorical variable) and previous preterm occurrences.

Figure Legends

Figure 1. Map of the study area showing the location of a sample subset of mothers (randomly selected with the QGIS tool “random points”), the location of the ground air monitoring stations and the areas within and outside 30 km of an air temperature station (‘urban’ vs. ‘rural’ areas).

Figure 2. Map of the study area showing the residential location of a subset of mothers over the daily predicted air temperature (C°) 1x1 km grid averaged for the entire year of 2005.

Figure 1.

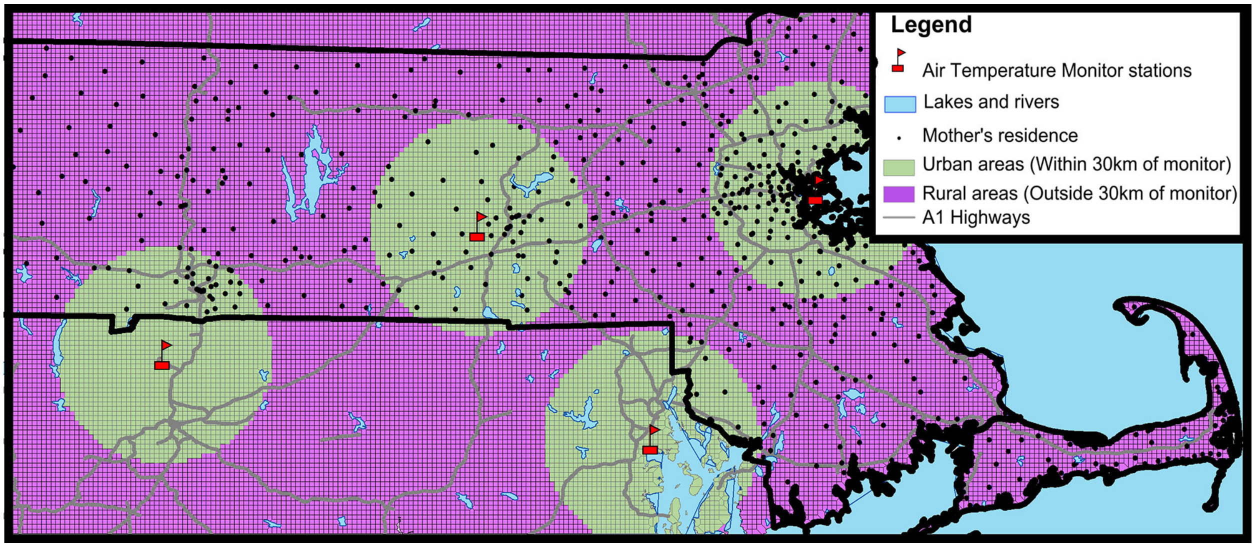
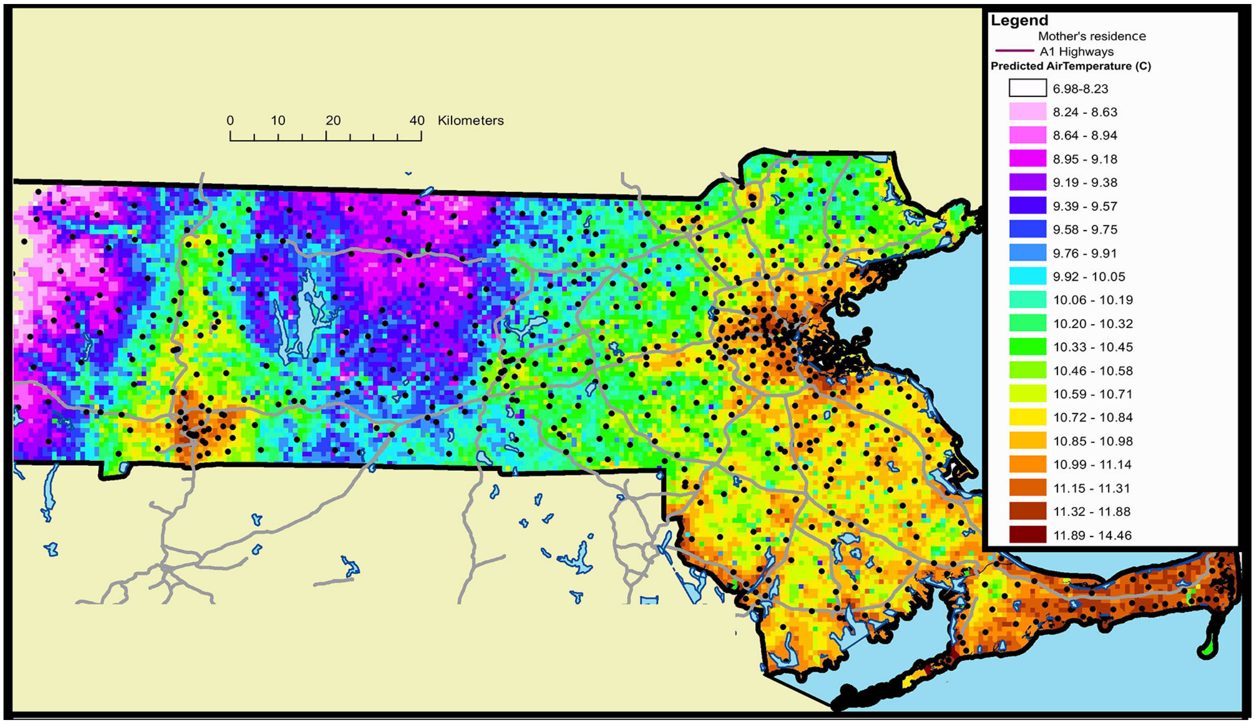

Legend
Air Temperature Monitor stations
Lakes and rivers
Mother's residence
Urban areas (Within 30km of monitor)
Rural areas (Outside 30km of monitor)
A1 Highways

Figure 2.


Legend
Mother's residence
A1 Highways
Predicted AirTemperature (C)
6.98-8.23
8.24 - 8.63
8.64 - 8.94
8.95 - 9.18
9.19 - 9.38
9.39 - 9.57
9.58 - 9.75
9.76 - 9.91
9.92 - 10.05
10.06 - 10.19
10.20 - 10.32
10.33 - 10.45
10.46 - 10.58
10.59 - 10.71
10.72 - 10.84
10.85 - 10.98
10.99 - 11.14
11.15 - 11.31
11.32 - 11.88
11.89 - 14.46
0 10 20 40 Kilometers